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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/756,018	11/25/96	SEED	B 00786/284002

EXAMINER

HM12/0831

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ART UNIT	PAPER NUMBER
1644	16

DATE MAILED: 08/31/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 6/3/99

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 10, 12-14, 24-25 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 10, 12-14, 24-25 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s) _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-421-632/40206

DETAILED ACTION

1. Applicant's amendment, filed 6/3/99 (Paper No. 15), is acknowledged.
Claims 1-9, 11 and 15-23 have been canceled.
Claim 10 has been amended.
Claims 24-25 have been added.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 6/3/99 (Paper No. 15).
The rejections of record can be found in the previous Office Action (Paper No. 13).

3. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84.
Please see the form PTO-948 previously sent in Paper No. 13.
Applicant is reminded to change the Brief Description of the Drawings in accordance with these changes (see Views).
Formal drawings will be submitted upon the indication of allowable subject matter.

4. The previous rejection under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention with respect to the recitation of "artificial P-selectin ligand, ... consensus sequence for attachment of a sialyl Le^x moiety and an amino acid consensus sequence for attachment of a sulfate moiety ... P-selectin ligand" has been obviated by applicant's amended claims and arguments, filed 6/3/99 (Paper No. 15)

5. The previous rejection under 35 U.S.C. § 112, first and second paragraphs, with respect to the recitation of "artificial P-selectin ligand, ... consensus sequence for attachment of a sialyl Le^x moiety and an amino acid consensus sequence for attachment of a sulfate moiety ... P-selectin ligand" has been obviated by applicant's amended claims and arguments, filed 6/3/99 (Paper No. 15).

6. Claim 25 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "said polypeptide comprises I135 through S225 of the CD43 precursor sequence".
Applicant's reliance on pages 12, 16 and 18 and Figure 14 the specification is acknowledged. However, the reference to "I135" and this particular range of "I135 through S225" is not readily apparent in these sections of the specification.
Therefore, the specification as filed does not appear to provide sufficient written description for newly added claim 25. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. The failure to meet the written description requirement under 35 USC 112, first paragraph arises when the claims are changed after the filing date to change the scope of the disclosure, which does encompass setting forth subgeneric claims (see MPEP 2163.05). Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide for the written description of the amended limitations in the specification as filed. It is acknowledged that applicant's reliance on certain pages of the specification discloses "Ile" and "S225" residues; however applicant should provide clear support in the application as filed for "I135" and the particular range recited in newly added claim 25.

7. Claims 24 and 25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 24 is indefinite in the recitation of "consisting essentially of" because the metes and bounds of those structural elements that do not materially affect the basic characteristics of the "tyrosine sulfation site" is unclear and ambiguous. Further, it is noted that this limitation is defined by a SEQ ID NO.; therefore, it is unclear what is included in this closed limitation of a particular SEQ ID NO. Also, given the profound effects that other structural elements such as single amino acid changes or carbohydrate moieties can have on a compound; the characteristics of "consisting essentially of" are unknown.

B) Claim 25 is indefinite in the recitation of polypeptide comprises I135 through S225 of the CD43 precursor sequence" because the appropriate amino acid residue should be spelled out at least by a three letter amino acid code and the claim should include the appropriate SEQ ID NO.

C) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

8. Claims 10 and 12-14 and newly added claims 24-25 are rejected under 35 U.S.C. § 103 as being unpatentable over Larsen et al. (U.S. Patent No. 5,843,707) OR Sasaki et al. (J. Biol. Chem., 1994; 1449) OR Sako et al. (Cell, 1993) in view of Aruffo et al. (Cell, 1991) and Lowe et al. (U.S. patent No. 5,595,900) essentially for the reasons of record set forth in Paper No. 16.

Applicant's arguments, filed 6/3/99 (Paper No. 15), have been fully considered but are not found convincing.

Applicant argues that Larsen et al. is only directed towards naturally occurring sites for sulfation and glycosylation in contrast to the instant recitation of "non-naturally occurring positions"

However, Larsen et al. Teach nucleic acids encoding P-selectin ligands, including modified and altered forms thereof as well as the importance of carbohydrate and sulfation sites in selectin-mediated binding and structure (see entire document). Also, Larsen et al. teaches sulfated tyrosines at any or all of positions 46, 48, 51 as well as additional peptide immunogens may be generated by replacing tyrosine residues with sulfated tyrosine residues (see column 18, lines 9-20). Also, Examples 12-13 of Larsen et al. clearly shows the importance and contribution of modification to P-selectin ligands. Here, Larsen et al. Also teach the importance of CD43 residues encompassed by the claimed invention. There appears no objective evidence that such modifications taught by Larsen et al. are limited to only naturally occurring sites; given the teachings that such modifications to tyrosine contribute to P-selectin ligand functions.

Applicant argues that Aruffo et al. only teaches that sulfatides which are lipids are ligands of P-selectin. Even though Aruffo et al. teaches sulfatides; Aruffo et al. also teach the importance of sulfation sites for P-selectin binding by suppressing P-selectin binding via the sulfation suppression (see entire document). Such modifications for nucleic acids encoding P-selectin ligands would have been obvious to the ordinary artisan at the time the invention was made.

Applicant argues that Lowe et al. Teaches enzymes that post-translationally modify protein substrates and does not disclose nucleic acids encoding P-selectin ligands that contain sites for both glycosylation and sulfation. However, Lowe et al. teach providing nucleic acids that encode for glycosylation and sulfation sites in glycoproteins of interest (see column 14, paragraph 2, for example). Given the known importance of such glycosylation sites for P-selectin-mediated interactions; Such modifications for nucleic acids encoding P-selectin ligands would have been obvious to the ordinary artisan at the time the invention was made.

Applicant argues that Sasaki et al. And Sako et al. do not teach nor suggest the nucleic acids encoding P-selectin ligands encompassed by the claims. However, applicant acknowledges that Sasaki et al. does teach cloning of Fuc-TVII, which, in turn, increases the binding of cells to E-selectin. However, given Sasaki et al.'s teaching that selectin ligands could be modified to express carbohydrate moieties, as well as the nucleic acid, vector and cells that encode and express said modified ligands. As well as Sako et al.'s teaching that nucleic acid encoding P-selectin ligand as well as the importance of carbohydrate sites in selectin-mediated binding and structure; such modifications for nucleic acids encoding P-selectin ligands would have been obvious to the ordinary artisan at the time the invention was made.

As pointed out previously, it was known at the time the invention was made that both sialyl and sulfation sites and structures contributed to P-selectin binding. Given the importance of both sialyl and sulfation moieties to the affinity and avidity of P-selectin-mediated binding, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide such moieties to modified/altered P-selectin ligands. It is noted that Larsen et al. teach nucleic acids encoding various modified/altered P-selectin ligands, including fragments and fusion proteins thereof for various uses (see columns 8-18). The prior art also provided for nucleic acids that encode for glycosylation and sulfation sites in glycoproteins of interest (for example, See Lowe et al.; column 14, paragraph 2). Therefore, the ordinary artisan would have motivated and would have expected the provision for sialyl and sulfation sites at non-naturally occurring sites in the generation of various modified/altered P-selectin ligands either to provide for or to increase affinity/avidity of such molecules. For convenience and homogeneity, it would have obvious to provide such sites in the nucleic acids encoding said altered/modified P-selectin ligands. Given the convenience of such, it would have been obvious to the recognized the art-known importance of carbohydrates in such receptor-ligand interactions.

In addition, it would have been obvious to the ordinary artisan to provide such modifications encompassing sialyl Le^x determinants or sulfated determinants to affect receptor-ligand interactions in characterizing structure-function relationships between such receptor-ligand interactions as well as their use to modify such receptor-ligand interactions.

In considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968). See MPEP 2144.01

One of ordinary skill in the art at the time the invention was made would have been motivated to select nucleic acids encoding P-selectin ligands including immunoglobulin fusion proteins and to modify the expression of sialyl Le^x determinants and sulfated determinants on said organic molecules to determine and to provide their contributions in receptor-ligand interactions as well as to regulate said interactions. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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